

**The critical role of aromatic residues in the binding of the  
SARS-CoV-2 fusion peptide to phospholipid bilayer membrane**

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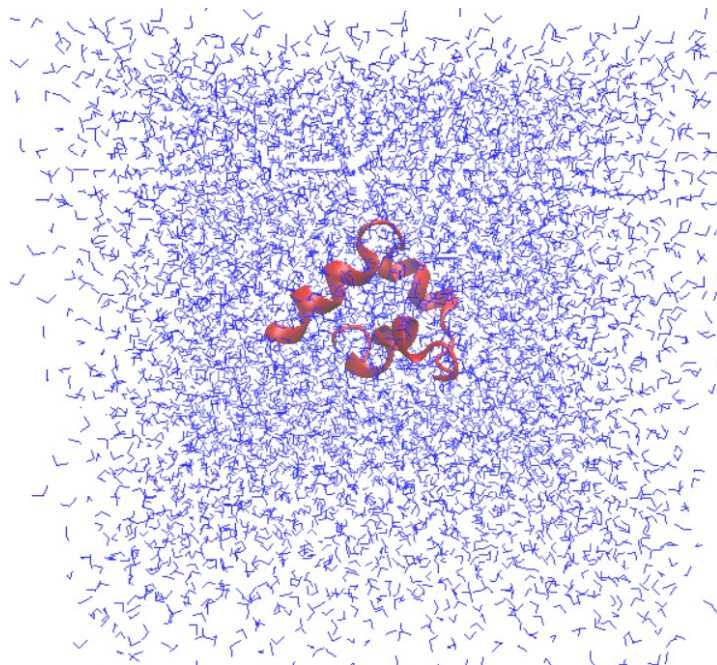
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**Supporting Information**

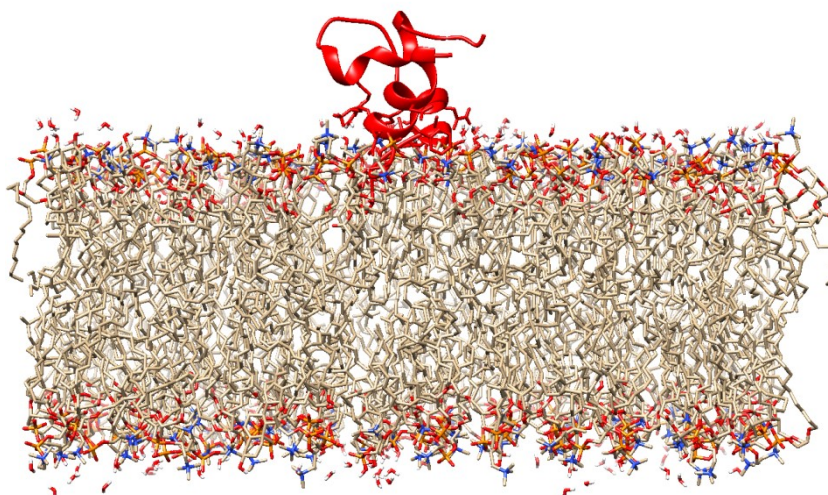
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**Figure S1.** Two representative FP models in (A) aqueous solution and (B) binding with the DMPC/DHPC/Cholesterol bilayer membrane.

(A)

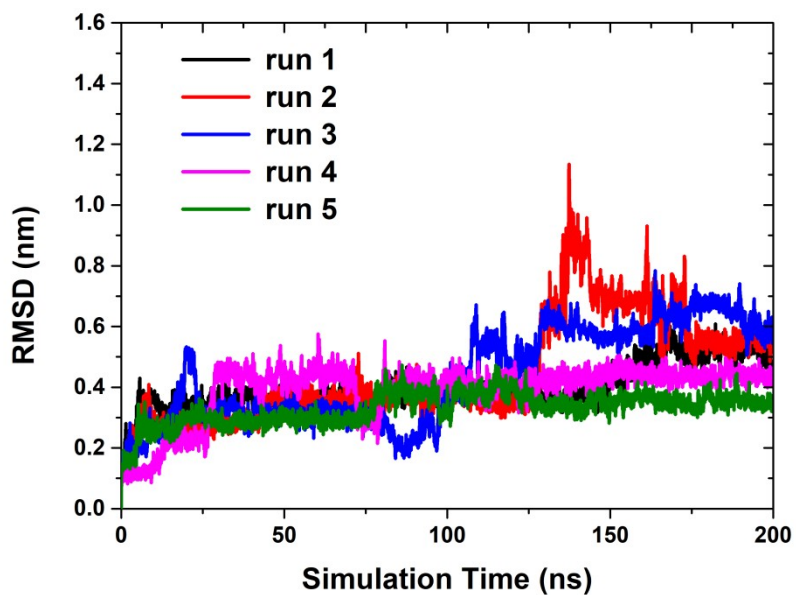


(B)

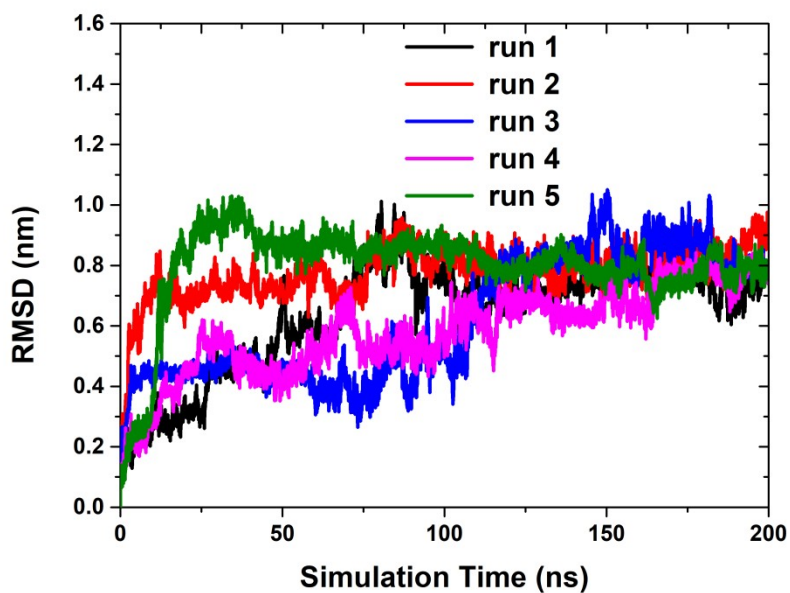


**Figure S2.** The RMSD results for the FP peptide bound to the cholesterol-free DMPC/DMPE bilayer in (A) the 0.15 M NaCl and (B) the 0.15 M CaCl<sub>2</sub> solution, obtained from five independent MD simulations.

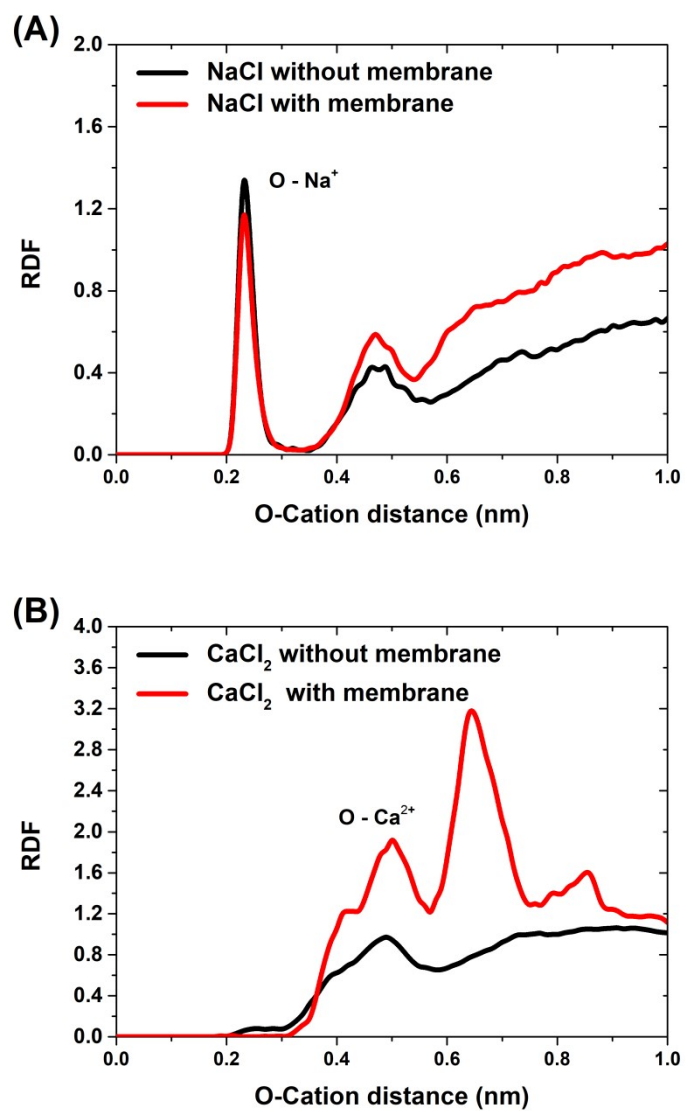
(A)



(B)

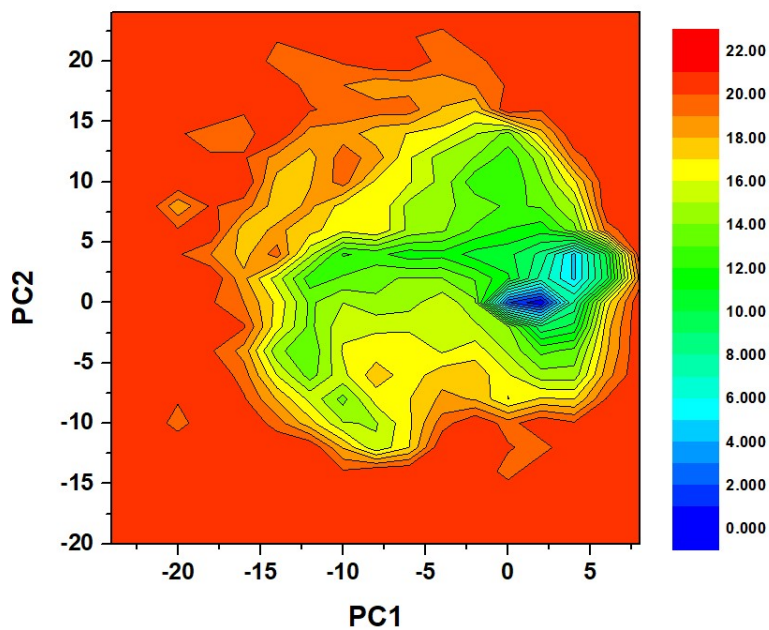


**Figure S3.** Radial distribution function (RDF) for the pairs formed between the oxygen atom of the peptide backbone and the ions, obtained from MD simulations of FP in the (A) NaCl (black) and (B) CaCl<sub>2</sub> (red) solutions without bilayer membrane (black) and with bilayer membrane (red).

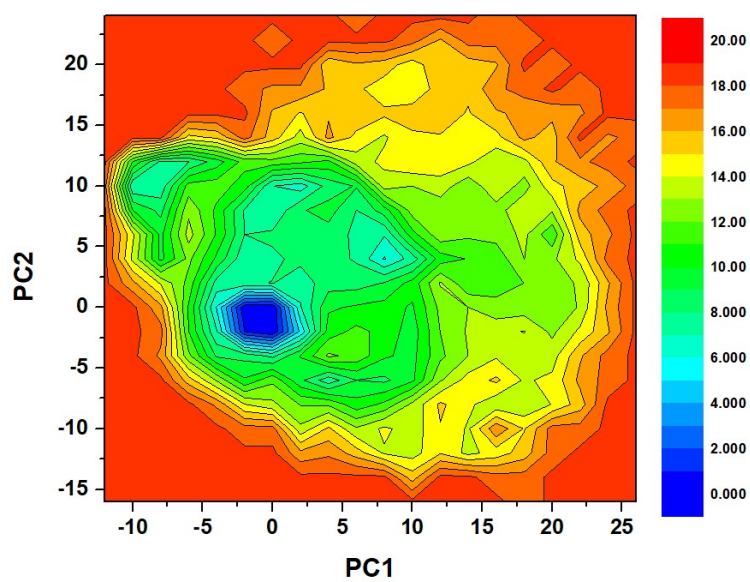


**Figure S4.** The PMF landscape (in unit of kJ/mol) profile of  $\Delta G(PC1, PC2)$  for the FP peptide bound to the cholesterol-free DMPC/DHPC bilayer membrane in (A) NaCl and (B)  $CaCl_2$  solutions.

(A)

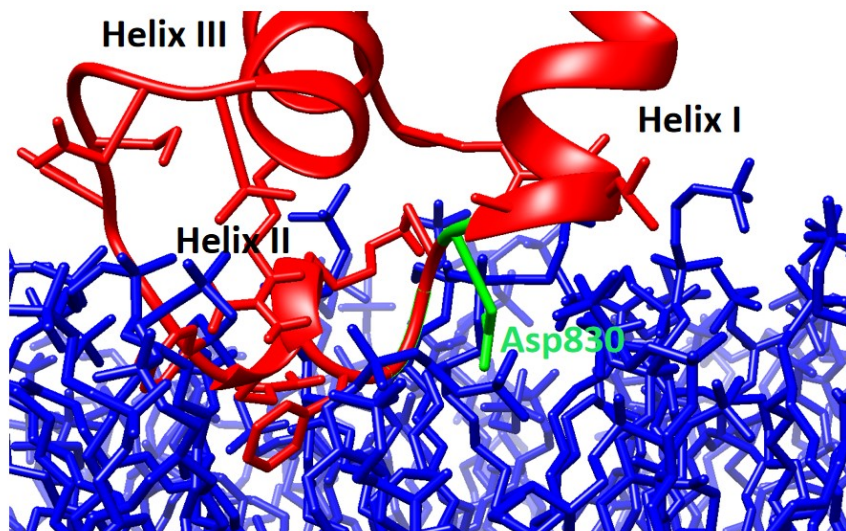


(B)

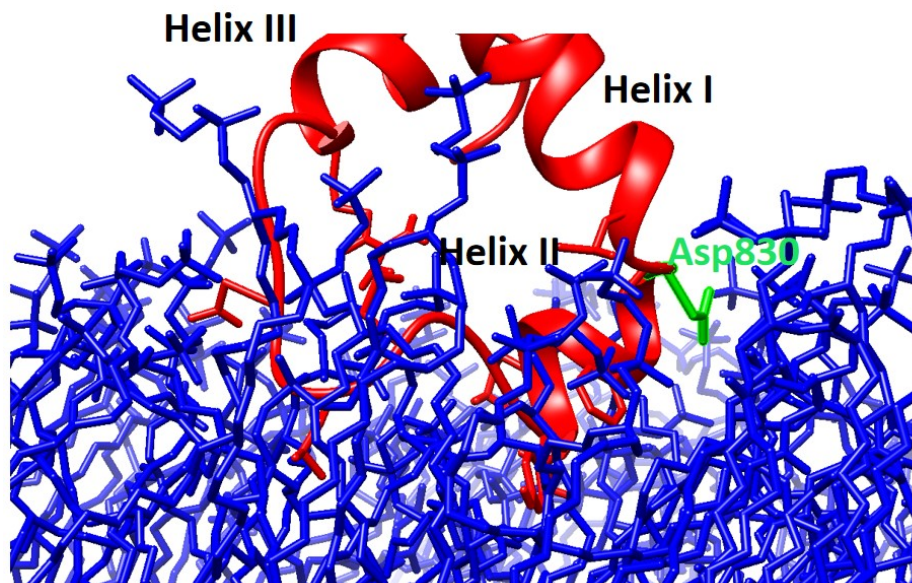


**Figure S5.** The most energetically favorable FP-membrane binding modes obtained from MD simulations of the FP binding to the cholesterol-free DMPC/DHPC bilayer membrane in (A) NaCl and (B) CaCl<sub>2</sub> solutions. Protein is illustrated in red and phospholipids in blue. The hydrophobic residue (Asp830) located between the helices I and II is represented in green.

(A)

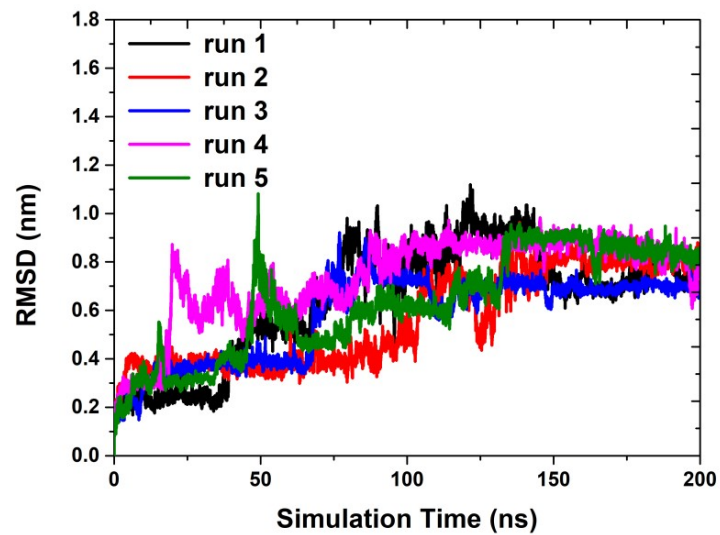


(B)

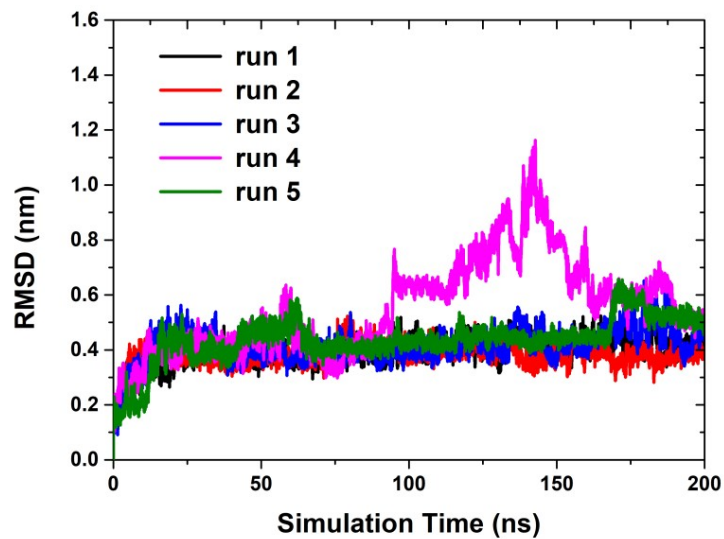


**Figure S6.** The RMSD results for the FP peptide bound to the DMPC/DMPE/cholesterol bilayer membrane in (A) the 0.15 M NaCl and (B) the 0.15 M CaCl<sub>2</sub> solution, obtained from five independent MD simulations.

(A)

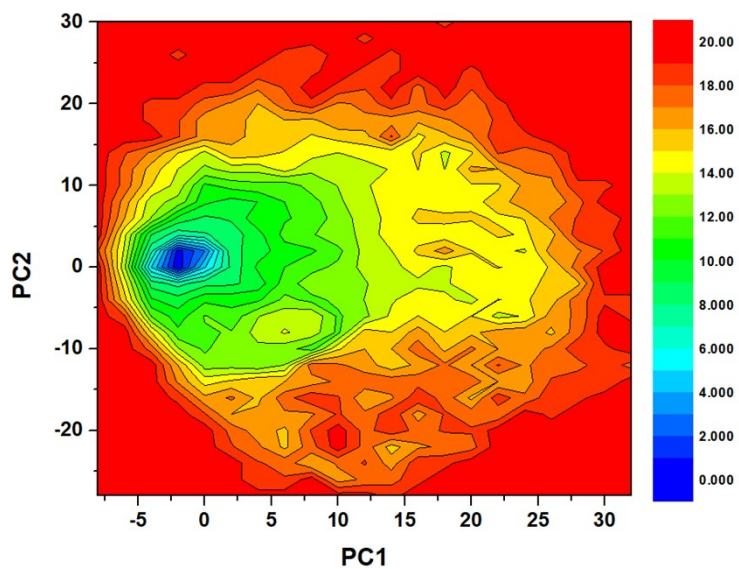


(B)



**Figure S7.** The PMF landscape (in unit of kJ/mol) profile of  $\Delta G(PC1, PC2)$  for the FP peptide bound to the cholesterol-riched DMPC/DHPC bilayer membrane in (A) NaCl and (B) CaCl<sub>2</sub> solutions.

(A)



(B)

